

CORRELATING FORMULATION PERFORMANCE WITH SOME PHYSICAL PROPERTIES OF α -CELLULOSE FROM CORN COB AND MELON HUSK-A COMPARATIVE STUDY.

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ABSTRACT

Alpha cellulose obtained as pulp from fibrous plant materials is used in pharmaceutical formulations as a disintegrant and a diluent for direct compression. This paper compares the performance of formulations prepared from local agricultural residues, namely melon husk and corn cob. The compression, compaction and disintegration characteristics of these materials were correlated with some physical properties and were compared to the well-known microcrystalline cellulose, Avicel PH 101. The results indicate that the good flow properties of α -cellulose from melon husks make it a better excipient in direct compression technology; while the compression behaviour and compactibility of α -cellulose from corn cob are superior in its dry-binding characteristics to that of melon husks though neither of these is equal in performance to Avicel PH 101. Compacts of all cellulose materials compressed to comparable porosity of 41-43 % disintegrated within 3 min, though appreciable differences exist among the cellulose materials. The observed differences in the two types of cellulose, even though the same extraction method was adopted, confirm literature reports that the properties of cellulose vary with the source type.

KEYWORDS: *Alpha* cellulose, microcrystalline cellulose, corn cob, melon husk, flow, compression, compaction and disintegration characteristics

INTRODUCTION

Environmentally friendly or green products are those that use less environmental resources, emit less pollutant to the different environmental media, use a substitute for genuine resources, utilize waste in the production of materials (resources recovery), and save energy used for industrial processes (Miller, 1992; Chiras, 1994; Kirkwood and Longley, 1995; Williams, 1998; Sherif *et al*, 2006). Furthermore, resource recovery is a new trend to achieve sustainable development. Wastes are considered secondary material resources and at the same time are renewable material resources.

Cellulose for industrial purposes is usually obtained from wood pulp and purified cotton linters. The need for environmentally friendly processes as well as the need to slow down the fast global deforestation has stimulated renewed interest in agro-fiber plants waste (Moore, 1996). It is against this background that corn cob and melon husks, which occur as huge agricultural waste in Nigeria, were investigated as sources for the production of α -cellulose production (Okhamafe *et al*, 1991, Ohwoavworhua *et al*, 2006). These studies have shown that α -cellulose obtained from these waste materials has potentials as a pharmaceutical excipient with excellent disintegrant and filler-binder properties in tablet formulations.

Formulation properties required for direct compression technology include good flowability, compactibility and compressibility. (Shlieout, 2000). This study therefore evaluates these properties for α -cellulose obtained from corn cob (CAC) and melon husk (MAC), compared to the well-known commercial microcrystalline cellulose, Avicel PH 101. The Kawakita (Yamashiro *et al*, 1983; Kawakita and Ludde, 1970/71) and Heckel (Heckel, 1961) models were used to assess these properties.

MATERIALS AND METHODS

Materials

These include nitric acid (Fisons, UK), sodium nitrite, sodium sulphite, sodium hydroxide (BDH, England), sodium hypochlorite (Reckitt and Colman Ltd., Nigeria), hydrogen peroxide (Fisons, England) and xylene (Vicker Laboratories Ltd., England). All other chemicals used were of analytical or reagent grade and water was double distilled.

Corn cob was collected from a farm in Idu, Abuja, Nigeria, while melon husk was obtained from a melon mill in Suleja, Nigeria.

Methods

Extraction of α - cellulose

The method reported in an earlier study (Ohwoavworhua, 2006), with slight modification, was used. The starting materials (corn cob and melon husks) were washed, dried at 60°C for 24 h and milled. The fraction passing through sieve 1.18 mm aperture size was used. A 300 g quantity each of the materials was treated with 4 L of 3.5 % nitric acid containing 40 mg of sodium nitrite for 2 h in a stainless steel container immersed in a water bath (FGL 1083, Karl Kolb Scientific) at 90°C to remove lignin in the form of soluble nitrolignins. Following thorough washing and filtration, it was digested with a 3 L solution containing 2 % w/v each of sodium hydroxide and sodium sulphite at a temperature of 50°C for 1 h. Again, it was washed, filtered and bleached with a 2 L 1:1 aqueous dilution of 3.5 % w/v sodium hydroxide at boiling temperature for 0.5 h. The washed and filtered material (i.e., holocellulose) was next treated with 2 L of 17.5 % w/v sodium hydroxide at 80°C for 0.5 h. The resulting α -cellulose was washed thoroughly with water. The extraction process was then completed by whitening with 1.5L of 6% hydrogen peroxide at 40°C for 2h and subsequent washing with water until the supernatant was clear. The cellulose material was filtered, and the water manually squeezed out to obtain small lumps, which were dried at 60°C in a fluidized bed dryer. Following further milling, and sieving the fraction of particle size \leq 600 μm was used for further investigation.

Fundamental powder properties

(a) Microscopy

A Nikon AFX -DX microscope (Nikon Inc., Japan) was used for preliminary assessment of the nature of particles in the cellulose materials. Each of the samples was mounted in glycerol and a combination of low and high power objective lenses of x 100 and x 400 magnification, respectively, were used.

(b) Particle size analysis

A sieve-shaker, (Retak 3D, Retsch GmbH and Co KG, Haan, Germany) was used for this assessment. Test sieves ranging from 650 to 150 μm were arranged in descending order. An 80 g quantity of powder sample was placed on the top sieve and the set-up was shaken at an amplitude of 1.50 mm/g for 5 min. The weight of material retained on each sieve was determined. The average diameter was computed as reported by Ansel *et al* (2005) using the following equation:

$$\text{Average diameter} = [\sum (\% \text{ retained}) \times (\text{mean aperture})]/100 \quad \dots (1)$$

(c) Particle density

The densities of the cellulose powders were determined by the liquid displacement method using xylene as the immersion fluid (Okhamafe *et al*, 1991), and the particle density, D_p , computed according to the following equation:

$$D_p = \frac{w}{[(a + w) - b]} \times SG \quad \dots (2)$$

Where w is the weight of powder, SG is specific gravity of solvent, a is weight of bottle + solvent and b is weight of bottle + solvent + powder.

(d) Bulk density

The bulk density of each cellulose material at zero pressure (loose density) was determined by pouring 30g quantity of the powder sample into a 250 ml measuring cylinder and the volume, V_0 , determined. The bulk density was calculated as $B_d = W/V_0$. The results presented are the mean of three replicate determinations.

Flow properties

Flowability was determined using Kawakita analysis (Yamashiro *et al*, 1983; Kawakita and Ludde, 1970/71). Tapped density was determined using Stampfvolumeter model STAV 2003 (JEF, Germany) – a modified Neuman apparatus (Neuman, 1967). Essentially, the method involved pouring a 30g quantity, each of the cellulose materials through an angle of 45^0 into a 250 ml glass measuring cylinder and the heap of the particles in the cylinder was leveled off horizontally by a thin metallic spatula and the bulk volume (V_0) was read. The cylinder was then mechanically tapped and values for the volume of the powder column (V) after a different number of taps N were determined. Three measurements were taken and the constants of this linear equation were calculated separately using tapping numbers below 30 and 10 observation points according to the method of least squares. The behaviour of both cellulose powders in the tapping procedure were compared using numerical constants obtained from the Kawakita plots.

The Kawakita equation for tapping experiments (Yamashiro *et al*, 1983; Kawakita and Ludde, 1970/71), which is used for assessing the flow properties of powders is:

$$\frac{N}{C} = \frac{N}{a} + \frac{1}{ab} \quad \dots (3)$$

Where a and b are constants; a describes the degree of volume reduction at the limit of tapping and is called the compactibility; $1/b$ is considered to be a constant related to cohesion and is called cohesiveness.

C , the degree of volume reduction is calculated from the initial volume V_0 and tapped volume V as:

$$C = \frac{(V_0 - V)}{V} \quad \dots (4)$$

Numerical values for constants a and $1/b$ are obtained from the slope, $1/a$ and the intercept, $1/b$, of plots of N/C against number of taps N .

Compaction studies

Preparation of compacts

Compacts of weights 400mg of each of the cellulose materials were made using a single station tablet press (Tianxiang Chentai Pharm. Machinery Co. Ltd., China) with a dwell time of 1 minute at compression pressures of 7 to 14 units, corresponding to the compression pressures of 17.5 to 35.0 KN, respectively. Forty tablets were made at each compression level.

Before compression, the die (10.5 mm diameter) and the flat-faced punches were lubricated with a 2 % w/v dispersion of magnesium stearate in ethanol-ether (1:1). The compacts were stored over silica gel for 24 h (to allow for elastic recovery and hardening and prevent falsely low yield values) before evaluation. The dimensions {thickness (h) and diameter (D)} and weight uniformity of ten compacts were determined. The compact diametral crushing strength (C_s) was determined using an Erweka hardness tester (model MT, Germany). The relative density D was calculated as the ratio of density of the compact, D_t , to the particle density, D_p , of the cellulose powder. The density of the compact was calculated from the ratio of the compact mass to the volume of the compact. The volume of the compact at a given pressure was calculated according to the equation: $V = \pi r^2 h$, where V is the volume, r is

the radius, and h is the thickness of the compact. The data obtained using this ‘ejected tablet method’ was used to obtain the Heckel plots and linear regression analysis was carried out over a compression range of 22.5 to 30.0 KN to determine the parameters from the plots.

The Heckel (Heckel, 1961) equation is:

$$\ln 1/(1-D) = KP + A \quad \dots\dots(5)$$

Where D is the density of the compact relative to the particle density of the material being compacted, P is the applied pressure, K (the slope of the straight line portion) is the reciprocal of the yield pressure, P_y , of the material. The yield pressure is inversely related to the ability of the material to deform plastically under pressure and A is a function of the original compact volume. From the intercept A , the relative density D_a , can be calculated using the equation 5:

$$D_a = 1 - e^{-A} \quad \dots\dots(6)$$

The relative density D_0 , of the powder at the point when the applied pressure equals zero (D_0 = loose density/particle density) is used to describe the initial rearrangement phase of densification as a result of die filling and high value indicating very dense packing.

The relative density D_b , describes the phase of arrangement during the initial stages of compression. The extent of this depends on the theoretical point of densification at which particle deformation begins. D_b is obtained from the difference between D_a and D_0 .

$$D_b = D_a - D_0 \quad \dots\dots(7)$$

The tensile strength (Ts) was calculated using the Fell and Newton’s expression (Fell and Newton, 1970).

$$Ts = 2C_s/\pi Dh \quad \dots\dots(8)$$

The tensile strength values were then plotted against the respective compression pressures. The area under the tensile strength versus compression pressure curves (AUTSC) was calculated by the trapezoidal method. This is a measure of the compactibility of the material (ie, strength of the tablets) (Habib *et al*, 1996).

Disintegration Studies

The disintegration test was performed in water at 37°C using an Erweka disintegration apparatus. The disintegration times reported are averages of 6 determinations.

Table 1: Some Fundamental Properties of CAC, MAC and Avicel PH 101 Powder Samples

Properties	CAC	MAC	Avicel PH 101
<i>Nature of particles</i>	Highly composed of aggregates which are irregular in shape.	Composed of few large aggregates which are irregular.	Composed of primary particles which are fibre-like.
<i>Average particle diameter (μm)</i>	196.4	224.0	50
<i>Particle density (g/ml)</i>	1.31 ± 0.06	1.44 ± 0.08	1.47 ± 0.02
<i>Bulk density (g/ml)</i>	0.24 ± 0.0	0.46 ± 0.04	0.31 ± 0.04

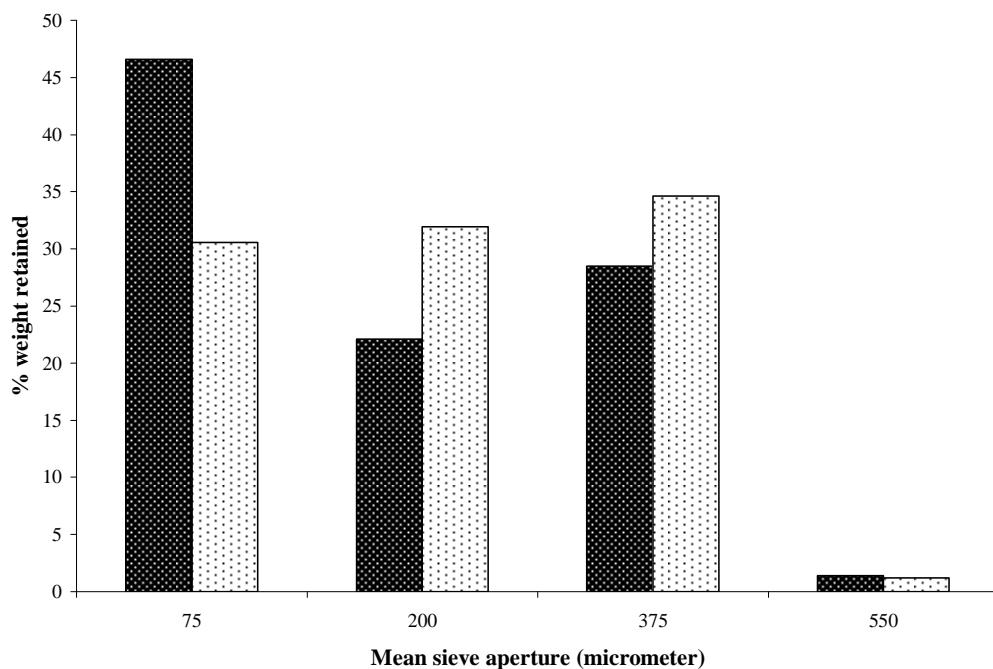


Figure 1: Particle size distribution for the α -cellulose, MAC () and CAC ()

RESULTS AND DISCUSSIONS

The fundamental properties of the cellulose powders are shown in Table 1, while Figure 1 shows the particle size distribution for CAC and MAC powders.

Flow properties

The Kawakita plots for CAC, MAC and Avicel PH 101 powders gave the linear relationship shown in Figure 2. The parameter values obtained from these plots indicate that the cellulose materials densified differently as shown by the compactability, a , values (Table 2) and attained the final packing state at different densification rates as indicated by the cohesiveness, I/b , values (Table 2). The order of compactability was CAC \approx Avicel PH 101 > MAC. Yamashiro *et al*, (1983) have reported an inverse relationship between powder compactability and fluidity. Consequently, the MAC powder with a low compactability value would be expected to have better fluidity. The larger particle size of MAC (Table 1) could have exerted granule effects by promoting better fluidity. The cohesiveness values for the CAC and Avicel PH 101 were found to be comparable and higher than for MAC powder. It is possible that the higher proportion (about 46 %) of 'fines' for CAC (Figure 1) and Avicel PH 101 (Table 1) accounted for the observed cohesiveness. The relatively lower cohesiveness obtained for MAC agrees with the earlier inference that its low compactability would result in good fluidity. The compactability and cohesiveness values obtained for MAC indicate fair flowability and moderate cohesiveness ((Neuman 1967, Shlieout *et al*, 2000). It would therefore be expected to be useful in the production of tablets from drug substances with moderate flow properties where the need of a glidant might be eliminated or reduced.

Compaction properties

Powder compaction is a volume reduction process, and the Heckel equation (Okhamafe *et al* 1991) is also based on volume change of a powder column during compression. The plots gave a general impression of the densification process of the powder column. The Heckel plots for the cellulose materials are shown in Figure 3.

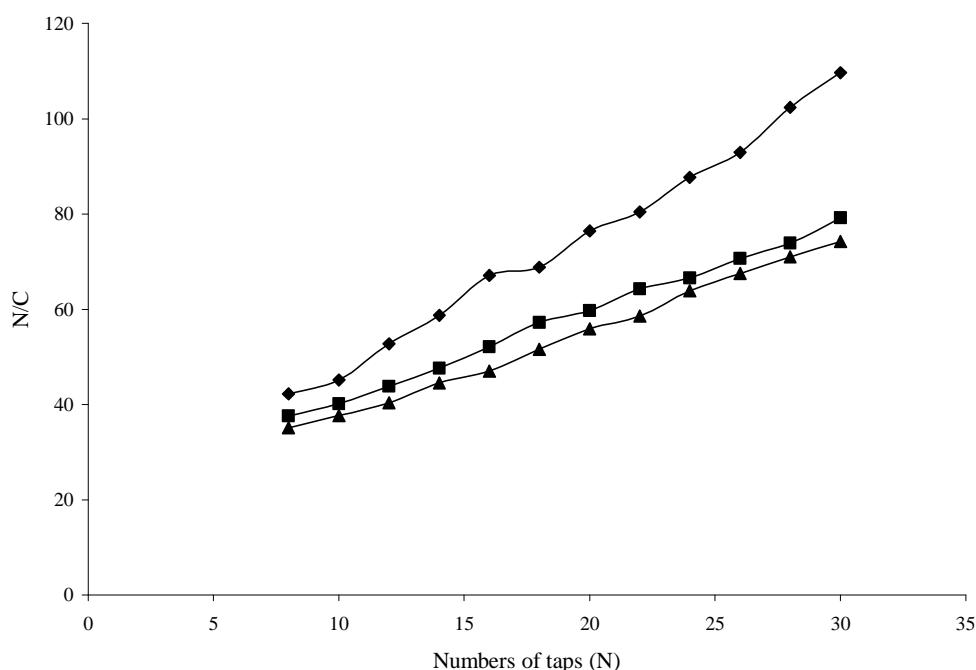


Figure 2: Kawakita plots for the cellulose powders, MAC (♦), CAC (■) and Avicel PH 101(▲).

Table 2: Parameters from Kawakita Plots

Characteristics	CAC	MAC	Avicel PH 101
Compactibility a (%)	53	33	54
Cohesiveness I/b	11.53	5.36	10.26

Table 3: Parameters Derived from Density Measurements and Heckel Plots for CAC, MAC and Avicel PH 101 Excipients

Cellulose type	Parameters							
	R ²	AUHC (KN)	AUTSC (M N/m ² . KN)	K	P _y (KN)	D _a	D _o	D _b
CAC	0.9194	23.23	2.801	0.1863	5.368	0.2744	0.1832	0.0912
MAC	0.9701	18.76	1.729	0.1268	7.886	0.4385	0.3194	0.1191
Avicel PH 101	0.9669	18.71	3.759	0.1225	8.163	0.4606	0.2497	0.2497

D_o = Relative density of powder or densification due to die filling

D_a = Densification due to die filling and rearrangement

D_b = Densification due to rearrangement

Table 4: Tensile Strength and Disintegration of CAC, MAC and Avicel Compacts

Product	Porosity (%)	Tensile Strength (M N/m ²)	Disintegration Time (seconds)
Avicel PH 101	43	0.0878	89
MAC	43	0.0181	5
CAC	41	0.0418	141

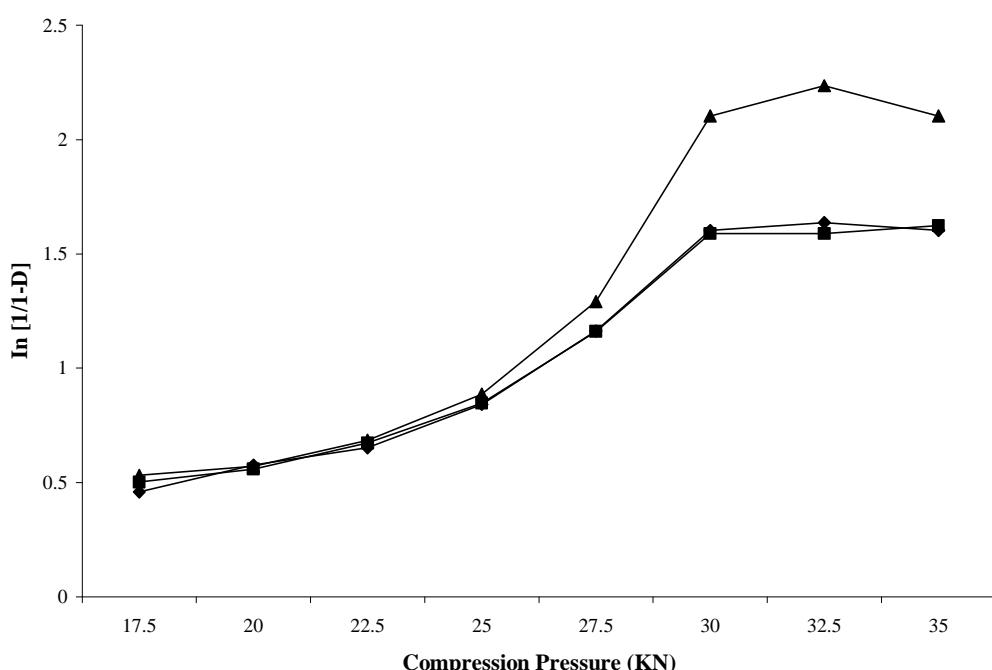


Figure 3: The Heckel plots for MAC (\diamond), CAC (\blacktriangle) and Avicel PH 101(\blacksquare) excipients.

To explain the deformation characteristic of α -cellulose, Heckel constants as well as area under the Heckel curve, AUHC, were derived from the plots (Table 3). The powder column formed by MAC was more densely packed than those of Avicel and CAC in the initial stages of rearrangement as indicated by their D_o values (Table 3).

The low D_a value for CAC powder is an indication that it opposes the densification process less strongly than MAC and Avicel. Paronen and Juslin (1983) stated that D_a describes the share of densification due to contact area between particles; therefore, the low D_a value of CAC is an indication of low contact area between the particles. This is expected as it is highly composed of aggregates resulting in low surface area and hence low contact area. In contrast, the value for MAC is higher, even though it is composed predominantly of aggregates particles with average size of 224 μm . This is probably due to fragmentation of its aggregates resulting in higher contact area. It has however been reported that the resultant contact area in a powder bed is dependent upon the interplay of several variables ranging from specific surface area (sequel to particle size), particle size distribution, particle shape to surface

properties of the powders such as hardness of the surface. The effect of any of these variables is difficult to distinguish (Stamm, 1964).

D_b , which describes the phase of rearrangement of particles, the extent of which depends on the theoretical point of densification at which deformation begins, was also determined for the powders. Avicel has the highest value, followed by MAC and then CAC. This is the reverse of the order for D_a , which is an indication that CAC particles were more resistant to movement once the initial phase of packing as a result of die filling had been completed. This could be attributed to high proportion of ‘fines’ (Figure 1) resulting in strong cohesive forces.

The mean yield pressure, P_y , which is inversely related to the ability of the material to deform plastically under pressure¹⁷, was found to be lowest for CAC (Table 3). The results therefore indicate that CAC underwent plastic deformation more easily and rapidly than MAC and Avicel PH 101 whose P_y values are comparable.

The greater compressibility of CAC compared to MAC and Avicel is also evident from the AUHC values (Table 3). The mean yield pressure, P_y and AUHC results show that CAC is more ductile material than the others. Kumar *et al* (2001) have reported that a coefficient of determination (R^2) value close to unity is indicative of plastic deformation, whereas decreasing values suggest fragmentation propensity. The R^2 values would seem to indicate that CAC also has a tendency to fragmentation. CAC is therefore an interesting material requiring further investigation as it seems to combine malleability with fragmentation¹⁸.

The relationship between tensile strengths of the cellulose materials and the respective compression pressures is shown in Figure 4. As expected, the tensile strength of the compacts increased with increased in compression pressure indicating the formation of more and strong bonds. The extent of increase was higher at the lower pressures as more new bonds would be formed at lower pressures. As the pressure increased over 30- 35 KN, only a small change in tensile strength was noted. MAC and CAC compacts exhibited a slight decrease over compressional pressures of 30-32.5 and 32.5-35.0 KN respectively. It is explained that this is probably due to the destruction of some bonds as a result of excessive pressure or break up after removal of pressure. The AUSTC shows that Avicel has highest compactibility, followed by CAC and then MAC. The observed compactibility of Avicel, is due to its relatively more crystalline nature compared to α -cellulose which is amorphous in nature.

The tensile strength and disintegration times of the cellulose compacts, compressed to a comparable porosity of 41-43% are presented in Table 4. As noted earlier, Avicel PH 101 formed the strongest tablets (compacts). The strength of Avicel, CAC and MAC compacts also followed the same trend, as for AUTSC values. Interestingly, all the compacts disintegrated within 3 min. However, it is observed that though they have comparable porosity their disintegration times were significantly different. This observation could be indicative of the fact that disintegration time may be affected significantly by factors other than porosity of compacts. Such factors may include intrinsic physicochemical characteristics of the cellulose material like degree of crystallinity which has been reported to affect rate of water uptake (William *et al*. 1998) In this respect, Van Kamp *et al*, (1986) observed, in a study of the dissolution and disintegration properties of different type of crystalline lactose, that the differences in water penetration and the consequent differences in disintegration behaviour among the lactose tablets should be explained by differences in their crystallinity (Yamashiro *et al*, 1983)

CONCLUSION

The results presented show that the flow, compression, compactibility and disintegration properties of the two types of α -cellulose are different. Since flow is a critical parameter in direct compression technology, the good flow properties of MAC make it a better diluent. The compression behaviour and compactibility data showed CAC to be a better dry binder. The observed differences in the two types of cellulose, although the same extraction method was adopted, confirm literature reports that the properties of cellulose vary with the source type.

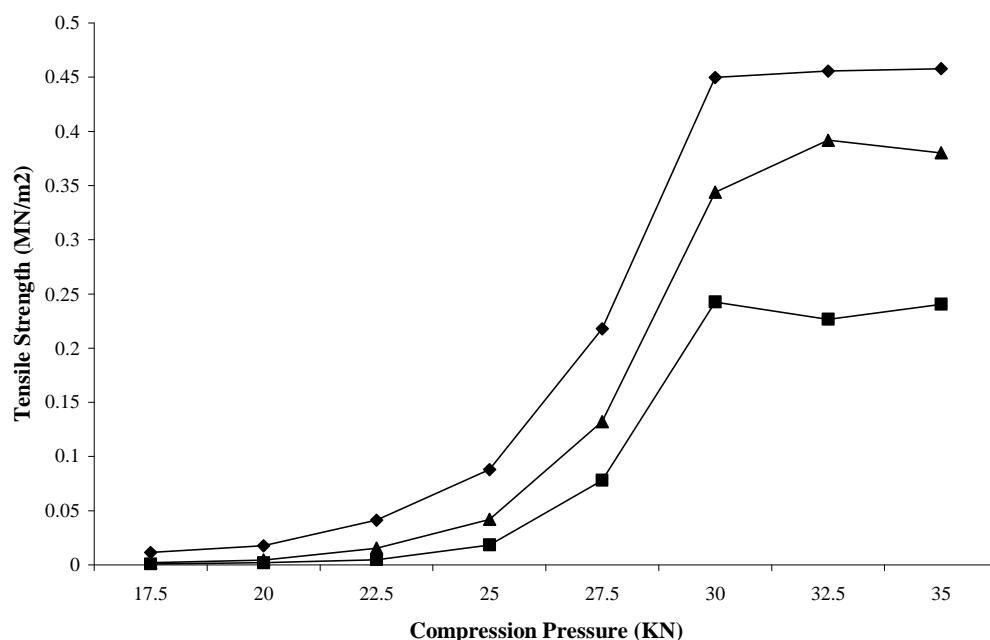


Figure 4: The relationship between tensile strength and the applied pressures for CAC (▲), MAC (■) and Avicel PH 101(◆) excipients

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